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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SLOBODYANSKY, ELIZABETH	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/527,376	LUCHE ET AL.	
	Examiner	Art Unit	
	Elizabeth Slobodyansky, PhD	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,7-14 and 51-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2 and 7* is/are allowed.

6)☒ Claim(s) *8-14 and 51-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed November 17, 2003 amending the specification to insert references to the sequence identifiers and delete citations of Internet website addresses, canceling claims 1 and 3-6, amending claims 2, 7, 8, 10, 11 and 14 and adding claims 51-59 has been entered.

Claims 2, 7-14 and 51-59 are pending.

Claim Objections

Claims 12 and 13 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. Claim 12 depends from claims 10 or 11 wherein claim 10 is a multiple dependent claim. Claim 13 depends from claim 12. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11, with dependent claims 12 and 13, and claims 51-56, with dependent claims 8-10, 14 and 57-59, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide encoding SEQ ID NO:2,

including SEQ ID NO:1 and degenerate variants thereof, does not reasonably provide enablement for a polynucleotide encoding a polypeptide capable of dephosphorylating an activated MAP-kinase that is at least 70%, 80% or 90% identical to a polynucleotide encoding an amino acid sequence set forth in SEQ ID NO:2, wherein said polypeptide comprises or does not comprise Asp73 and/or SEQ ID NO:3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The specification does not support the broad scope of the claims which encompass polynucleotides encoding a polypeptide capable of dephosphorylating an activated MAP-kinase that is at least 70%, 80% or 90% identical to SEQ ID NO:1 or any polynucleotide encoding an amino acid sequence set forth in SEQ ID NO:2, wherein said polypeptide comprises or does not comprise Asp73 and/or SEQ ID NO:3 because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting a DSP-2 activity; (B) the general tolerance of DSPs to

modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any DSP-2 residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The specification teaches a polynucleotide of SEQ ID NO:1 encoding a DSP-2 of 188 amino acids (SEQ ID NO:2). The active site domain of said DSP-2 is located at residues 102-111 of SEQ ID NO:2 (SEQ ID NO:3). However, a fragment corresponding to SEQ ID NO:3 is unlikely to exhibit DSP-2 activity and it constitutes about 5% of the amino acid structure. Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, beyond that provided in the specification, in order to make a polynucleotide encoding a polypeptide capable of dephosphorylating an activated MAP-kinase that is at least 70%, 80% or

90% identical to a polynucleotide encoding an amino acid sequence set forth in SEQ ID NO:2, wherein said polypeptide comprises or does not comprise Asp73 and/or SEQ ID NO:3 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-14 and 54-56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites a polynucleotide that both hybridizes to SEQ ID NO:1 "under conditions that include a wash in 0.1 X SSC and 0.1% SDS at 60°C for 15 minutes" and "exhibits at least 70% nucleotide identity to a polynucleotide comprising SEQ ID NO:1". The polynucleotides that will hybridize to SEQ ID NO:1 under the above conditions would have more than 70% nucleotide identity to SEQ ID NO:1. Therefore, the scope of the claimed product is unascertainable.

Claims 54-56 are confusing as drawn to "An isolated polynucleotide that encodes a polypeptide capable of dephosphorylating an activated mitogen-activated protein kinase (MAP-kinase), said polypeptide comprising an amino acid sequence of SEQ ID NO:2, wherein aspartic acid is located at positions 102 through 111 of SEQ ID NO:2, wherein said polynucleotide comprises a sequence at least 70% [80% or 90%] identical to a polynucleotide that encodes a polypeptide comprising the amino acid sequence of

SEQ ID NO:2" (emphasis added). As written, said claims are drawn to a polynucleotide that encodes SEQ ID NO:2 not a variant thereof as appears to be intended. In a polypeptide of SEQ ID NO:2 aspartic acid is located at position 73 and SEQ ID NO: 3 is located at positions 102-111. The recitation of these positions is redundant. It appears it was intended to recite a polynucleotide encoding a polypeptide having an amino acid sequence that differs from SEQ ID NO:2 by one or more deletions, additions or substitutions and comprises aspartic acid at position 73 and SEQ ID NO:3 at positions 102-111.

Claim 14 is unclear as drawn to a method of producing a DSP-2 whereas claims 51-56 which claim 14 depends from recite a polypeptide capable of dephosphorylating an activated mitogen-activated protein kinase (MAP-kinase).

Claims not specifically discussed in this rejection are rejected as dependent from a rejected base claim.

Allowable Subject Matter

Claims 2 and 7 are allowed.

Response to Arguments

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive.

The 112, 1st paragraph, written description rejection is obviated by the amendment. The 102 and 103 rejections are obviated by the amendment.

With regard to the 112, 1st paragraph, enablement rejection, Applicants argue that "As taught in the specification, DSP-2 polynucleotides may comprise a native sequence or a variant of such a sequence (*see, e.g.*, page 9, line 3 through page 10, line 7). Such polynucleotide variants may occur as a result of the degeneracy of the genetic code" (Remarks, page 15). It is noted that degenerate variants of SEQ ID NO:1 are not rejected. Applicants further argue with regard to a sequence at least 70% identical to a polynucleotide that encodes SEQ ID NO:2 that "By using computer algorithms well known in the art and disclosed in the specification, such as Align or the BLAST algorithm, a person skilled in the art can determine the percent identity of a polynucleotide to the disclosed DSP-2 polynucleotide sequence" (page 15). Applicants further argue that "the polypeptide produced can then be routinely analyzed for its ability to dephosphorylate a suitable substrate such as an activated MAP-kinase (page 16). It is agreed that it is possible to determine the percent identity between two given sequences. However, the point of the rejection is different. It is related to how to make a variant sequence that will be aligned. The arguments are not persuasive because while methods to produce variants of a known sequence are well known to the skilled artisan producing variants as claimed by requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the great number of variants have the requisite activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the

specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. As stated above the specification does not establish: (A) regions of the protein structure which may be modified without affecting a DSP-2 activity; (B) the general tolerance of DSPs to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any DSP-2 residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky, PhD whose telephone number is 571-272-0941. The examiner can normally be reached on M-F 10:00 - 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, PhD can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner
Art Unit 1652

February 13, 2004